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TEN YEARS OF MUSCLE RESEARCH IN HUNGARY

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Approximately half of the human body is composed of muscle tissue, and muscular action is involved in most human activities. Therefore, it is very important that the metabolism of healthy and ill humans be known. Also, the medical fields of labor physiology and sport hygiene require increasingly greater muscular research. Although the above pertains to striated muscle tissue, research on smooth muscle tissue is equally important because the activity of vital organs such as the intestines, the uterus, urinary bladder, arteries, etc, are controlled by smooth-muscle action. With the inclusion of the heart, with its peculiar composition and activity which combines both striated and smooth muscle characteristics, it becomes obvious why muscle research has been in the foreground since the earliest days of biological science and why muscle research is still one of the leading aspects of the entire field of experimental biology.

Whereas 2 exact sciences -- biophysics and biochemistry -- have evolved from the field of biology muscle research has been conducted chiefly along these lines because due to its past history and its peculiar characteristics muscle research has always been one of the most exact fields of biological research. This is true at present, also, although the nature of research problems do not permit the separation of the biochemical and biophysical aspects and truly great results can be achieved only through the combined operations of these two branches of science.

Considerable muscle research was done in Hungary before World War II and although this research was abreast of leading international muscle research it was isolated to a considerable degree from the other branches of scientific life of the country. Following the liberation, the new government, which favored scientific development, effected the formation of 2 muscle research centers: one of these was first formed under the leadership of Bruno Straub at Szeged and later moved to the Institute of Medical Chemistry of the Budapest Medical School, and the other was under the leadership of Jeno Ernst at the Institute of Biophysics of the Pecs Medical School. Significant work is muscle research also was done under the leadership of professor Lissak at the Pecs Institute of Biology, under professor Went at the Debrecen Institute of Biology, at the Institute of Biochemistry of the Hungarian Academy of Sciences under Szorenyi, and at the institute of the Eotvos Lorand University headed by Jendrassik. Two new research facilities which are active in the field of muscle research are the Institute of Animal Biochemistry of Eotvos Lorand University, which is headed by Endre Biro, and the Institute of Biochemistry at the Budapest Medical School, which is headed by Mrs. Vilma Hermann Szekessyne. On a par with the great increase in the number of institutes now engaged in muscle research is the increase in outstanding trained personnel in this field. These include Jozsef Tigyi of Pecs and Emil Varga of Debrecen, and many younger researchers who have joined in this excellent, very active field. Research possibilities and research results in this field are greatly assisted by the Electron Microscope Laboratory where, under the leadership of Ferenc Guba, work is being done on the study of muscle structure.

The brief survey of the developments within the field of muscle research give a hint of the magnitude of the progress which has been made, and a more detailed account of the achievements of the past 10 years would require a prohibitive amount of space merely for listing a complete bibliography. Therefore, it may be stated summarily that almost every number of the Acta Physiologica has carried an article pertaining to muscle research, and the latest results of muscle research are discussed at every meeting of the Hungarian Biological Society.

A considerable number of foreign delegations participated in the last meeting of this society. According to a recent letter from Koshtoyants the experiences of the Soviet delegation will soon be published, the account of the English delegation also cites the outstanding results achieved by Hungarian muscle research, and according to the opinion of professor Verzar, who has been at the University of Basle, Switzerland for 20 years, Hungarian muscle research is to be heartily congratulated for the results it has achieved.

Turning to the most outstanding results achieved, in the field of biochemistry the theoretical principles of Engelhardt were further developed. It is well known that the Szent-Gyorgyi school developed the miosin-ATP question in detail, in the course of which Straub demonstrated that a protein body named actin is an important component of muscle tissue. These achievements gave impetus to intense world-wide research along this line, including continuation of this work by Hungarian researchers. Straub and his associates established that various cations which are mentioned in muscle research literature effect the speed of polymerization of actin, and that the antagonistic effects known in the field of physiology also effect this simple protein system (Ca-Na antagonism). They demonstrated the presence of a substance in actin which had a slightly beneficial effect on the activity of hypodynamic frog heart (weakened with chinin). Isolation of this substance revealed it to be identical with adenosintriphosfate (ATP), the role of which in muscle contraction has been known since 1939. The investigations showed that actin in the bound state contains ATP and that the bound ATP is broken down when the actin polymerizes. Through many experimental studies it was attempted to show that this dissociation is reversible and has a cyclical role in normal muscle function, but these experiments still have not led to a conclusive result. Investigation of enzymatic dissociation of ATP in actin led to the discovery that the known ATP-consuming enzymes (hexokinase, miokinase, creatinphosfoferase) as present only as pollutants and therefore the splitting-off of ATP in connection with polymerization is not due to enzyme action but is an entirely new process related to the physical change of the protein.

In the opinion of the author the conclusions of the Straub group pertaining to these experimental results arevery important. According to this group "the current trend in research is based on a misconception: that of considering muscular contraction to be an enzymatic process." The author views with satisfaction the fact that one of the outstanding exponents of the "biochemical theory" of muscular contraction expresses an opinion which is in complete agreement with the longstanding and oft-repeated viewpoint of the present author.

Another theoretically important opinion of Straub is the following: " ... any mechanical change which is accompanied by a change in the protein molecule also causes a change in the chemical composition, and the mechanical work which results in depolymerization of fibrous actin also produces chemical energy by producing ATP from ADP." This opinion considerably surpasses the Engelhardt conception of the mechanical-chemical connection, in that it allows for the possibility that the work

which is devoted to mechanical change of muscle tissue may result in the production of chemical energy and in chemical change. It is worthy of mention that Straub submitted this article in June 1949, and that A. V. Hill stated the following at the Eighteenth International Biological Congress in August 1950: "much of the work which is performed (on a contracted muscle) is lost, or rather, cannot be found as heat nor as potential mechanical energy. It is probable that this work is absorbed, in the course of which it reverses some chemical reaction." Thus Hill completely adopts Straub's idea without giving the latter credit. Hill maintains this attitude by citing as the experimental basis of this conception the fact that no elastic potential energy is produced in the extension (to a certain degree) of a contracted muscle, and the work which was put in cannot be found, and does not give credit to the present author, who first stated this fact in 1935.

The Institute of Biophysics of the Pecs Medical School has been active in the field of biophysical muscle research. The chief results of this work are the following:

1. It was shown that swelling, as well solutions play an important role in the water balance of muscle tissue. This does not mean, however, that the muscle is comparable to a swollen sac, especially since not all substances are present in muscle tissue in a freely diffusible state, for example K.

2. Through experimentation the hypothesis was formulated that miosin, similar to rubber, crystallizes under compression, which increases its solidity. It was postulated that this kind of process arises during muscular exertions. This process was termed "the automatic part of muscular activity."

3. The most outstanding work done by this institute seems to be the settling of the 30-year debate between Ernst and Meyerhof. According to Ernst one of the cardinal phenomena of muscle action is the fact first discovered by him, that the initial, rapid decrease in muscle volume is proportionate and parallel to, and simultaneous with the activating current. During the course of the long years of debate Meyerhof corrected his standpoint in many respects to conform with Ernst's data, but he effectively contradicted the conclusions of the latter pertaining to the activating current and decrease in volume. Through utilization of the new, great facilities which have become available since the Liberation the Institute developed new methods based on new principles, through which it was established that in the preliminary stage of muscle action decrease in volume is proportionate to the actuating current. This established a concrete fact in the research on the initial phase of muscle action, and established the electrical nature of the latter.

Another important achievement of the Pecs Institute of Biophysics is the setting up of a microcalorimeter laboratory by Jozsef Tigyi. This laboratory already has produced initial results of interest. These include gradual progress on a method which is being developed by Lajos Beleczki, in which formalin crystalizes on the surface of pre-formed structures, with an excellent demonstration of the longitudinal and latitudinal formations of individual fibrils of negative double-refracting "Formalin threads."

Muscle research at the Institute of Biochemistry of the Hungarian Academy of Sciences under Gyorgy Feuer is concerned chiefly with the problems of actin, miosin and ATP. The most recent findings of this

institute showed that ATP breaks down even with the effect of purely passive mechanical compression.

Lorant Jendrassik and his associates at the Department of Experimental Biology and Biological Chemistry at the Budapest University have been concerned chiefly with investigation of the process of muscle stimulation in connection with sarcolemma, and with changes in the water-, and muscular relationships of muscle tissue. The institute headed by Endre Biro also has done promising work which is aimed at analysis of the essence of muscle activity through study of protein-bound ATP, and the precise, excellent work being done by Mrs. Szekessyne has contributed greatly to the fund of data on the enzyme problem.

Kalman Lissak, Andras Angyan, and Elemer Endroczi and their associates at the Pecs Institute of Biology have performed numerous experiments on various problems of muscle activity, one of the most outstanding of which is the evoking of the clasping reflex in a winter frog through the use of chorion-gonadotrophin. Another outstanding achievement of this group is the production of a lasting improvement in myotonic patients. Research at the Debrecen Institute of Biology under Emil Varga is concerned chiefly with the acetylcholine-miosin-ATP linkage and on the therapeutic effects of ATP in muscular atrophy. Many valuable results have been attained in the latter field.

In addition to the great support of the government, the results which have been achieved in the field of muscle research also have been furthered by the organizational work of the Hungarian Academy of Sciences, which has made exchange of information possible through meetings and conferences, and which, at the suggestion of the present author, initiated the practice of sectional meetings which also have been very beneficial. It is the opinion of the author that further excellent results may be expected if muscle researchers were to discuss individual problems with specialists in certain fields at the present boundaries of science.

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